(FILE 'USPAT' ENTERED AT 08:06:41 ON 07 JUL 1998)
L1 48 S (PROSTHE? OR DEVIC? OR (TUBUL? (7A) IMPLANT?)) AND (PORE
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45. 5,131,907, Jul. 21, 1992, Method of treating a synthetic naturally occurring surface with a collagen laminate to support microvascular endothelial cell growth, and the surface itself; Stuart K. Williams, et al., 600/36; 424/93.7; 427/534, 538; 435/1.1, 375, 399; 623/1 [IMAGE AVAILABLE]

43. 5,171,261, Dec. 15, 1992, Vascular **prosthesis**, manufacturing method of the same, and substrate for vascular prothesis; Yasuhara Noishiki, et al., 623/1; 600/36 [IMAGE AVAILABLE]

38. 5,336,615, Aug. 9, 1994, Genetically engineered endothelial cells exhibiting enhanced migration and plasminogen activator activity; Leonard Bell, et al., 424/423, 93.21; 435/172.3, 320.1, 366; 600/36; 623/1; 935/70, 71 [IMAGE AVAILABLE]

34. 5,401,832, Mar. 28, 1995, Brain derived and recombinant acidic fibroblast growth factor; David L. Linemeyer, et al., 530/399, 402 [IMAGE AVAILABLE]

15. 5,628,781, May 13, 1997, Implant materials, methods of treating the surface of implants with microvascular endothelial cells, and the treated implants themselves; Stuart K. Williams, et al., 623/1; 424/93.21; 435/371; 623/11 [IMAGE AVAILABLE]

L10 ANSWER 1 OF 9 MEDLINE
AN 95211017 MEDLINE
TI Activities of granulocyte-macrophage colony-stimulating factor revealed by gene transfer and gene knockout studies.
AU Dranoff G; ***Mulligan R C***
CS Dana-Farber Cancer Institute, Boston, Massachusetts.
SO STEM CELLS, (1994) 12 Suppl 1 173-82; discussion 182-4. Ref: 65
Journal code: BN2. ISSN: 1066-5099.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 9507
AB We used retroviral mediated gene transfer and gene knockout technologies to explore the in vivo functions of murine granulocyte-macrophage colony-stimulating factor (GM-CSF) [1, 2]. In tumor vaccination experiments, GM-CSF was the most potent molecule of a large number of cytokines, adhesion molecules and other immunomodulators for the induction of specific and long-lasting anti-tumor immunity. Vaccination required activities of both CD4 and CD8 positive lymphocytes, and likely involved the augmentation by GM-CSF of host professional antigen-presenting cell function. Mice engineered by homologous recombination techniques in embryonic stem cells to lack GM-CSF demonstrated no significant perturbations in steady-state hematopoiesis. All mutant animals, however, developed the accumulation of surfactant proteins and lipids in the alveolar space, the defining feature of the idiopathic human disorder pulmonary alveolar proteinosis. Surfactant lipid and protein content were increased in the absence of alterations in surfactant protein mRNA, supporting the concept that surfactant clearance or catabolism was perturbed. Extensive lymphoid hyperplasia associated with lung airways and blood ***vessels*** was also found, yet no infectious agents could be isolated. These results demonstrate that GM-CSF is not an essential growth factor for basal hematopoiesis and reveal an unexpected, critical role for GM-CSF in pulmonary homeostasis. It is tempting to speculate that the ability of GM-CSF to modulate the uptake and processing of particulate material underlies the mechanisms of immunostimulation and surfactant accumulation.

L10 ANSWER 2 OF 9 MEDLINE
AN 94236778 MEDLINE
TI Efficient repopulation of denuded rabbit arteries with autologous ***genetically*** modified ***endothelial*** cells.

AU Conte M S; Birinyi L K; Miyata T; Fallon J T; Gold H K; Whittemore A D; ***Mulligan R C***
CS Whitehead Institute for Biomedical Research, Cambridge Center, MA 02142.
NC HL-41484 (NHLBI)
T32-GM-07560 (NIGMS)
HL-43771 (NHLBI)
SO CIRCULATION, (1994 May) 89 (5) 2161-9.
Journal code: DAW. ISSN: 0009-7322.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 9408
AB BACKGROUND: In an effort to determine whether specific ***genetic*** modifications of cells of the vascular system might improve the efficacy of existing clinical procedures such as endarterectomy, atherectomy, and percutaneous angioplasty, we investigated the utility of gene transfer to rapidly and efficiently repopulate injured arteries with ***genetically*** modified cells in an animal model. METHODS AND RESULTS: The method involves the harvest of autologous venous-derived ***endothelial*** cells, the efficient ***genetic*** modification of the cells through the use of recombinant retroviruses, and the subsequent implantation of the ***genetically*** modified cells on the surface of balloon-denuded arterial segments. With a rabbit model, freshly isolated ***endothelial*** cells were transduced with a recombinant retrovirus encoding the bacterial enzyme beta-galactosidase. The autologous transduced cells were then implanted on the surface of balloon-denuded ileofemoral arterial segments at different cell densities; after 1 to 14 days, the animals were killed, and the ***vessel*** segments were examined. Cells expressing the bacterial gene product, as determined by in situ staining for beta-galactosidase, were found to be present on the surface of 28 of the 32 arteries seeded with ***genetically*** modified cells. ***Vessels*** examined at 4 to 7 days after seeding displayed 40% to 90% coverage with transduced cells, even when seeded at subconfluent density, and an intact ***endothelial*** cell monolayer, as evidenced by scanning electron microscopy studies. ***Vessels*** examined at 14 days after seeding revealed more variable staining for beta-galactosidase yet, again, in most cases, an intact ***endothelial*** cell monolayer. CONCLUSIONS: These studies indicate the feasibility of generating segments of arterial ***vessels*** containing ***genetically*** modified cells in a rapid and efficient fashion. Further studies are now necessary to determine whether the local expression of specific polypeptides

within a region of ***vessel*** for a finite period of time will be clinically useful.

L10 ANSWER 3 OF 9 MEDLINE
AN 90296512 MEDLINE
TI ***Genetically*** modified ***endothelial*** cells in the treatment of human diseases.
AU Wilson J M; Birinyi L K; Salomon R N; Libby P; Callow A D; ***Mulligan R C***
CS Howard Hughes Medical Institute, University of Michigan Medical School, Ann Arbor 48109..
SO TRANSACTIONS OF THE ASSOCIATION OF AMERICAN PHYSICIANS, (1989) 102 139-47.
Journal code: W5P. ISSN: 0066-9458.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9010

L10 ANSWER 4 OF 9 MEDLINE
AN 89283716 MEDLINE
TI Implantation of vascular grafts lined with ***genetically*** modified ***endothelial*** cells.
AU Wilson J M; Birinyi L K; Salomon R N; Libby P; Callow A D; ***Mulligan R C***
CS Whitehead Institute, Cambridge, MA..
SO SCIENCE, (1989 Jun 16) 244 (4910) 1344-6.
Journal code: UJ7. ISSN: 0036-8075.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8909
AB The possibility of using the vascular ***endothelial*** cell as a target for gene replacement therapy was explored. Recombinant retroviruses were used to transduce the lacZ gene into ***endothelial*** cells harvested from mongrel dogs. Prosthetic vascular grafts seeded with the ***genetically*** modified cells were implanted as carotid interposition grafts into the dogs from which the original cells were harvested. Analysis of the graft 5 weeks after implantation revealed ***genetically*** modified ***endothelial*** cells lining the luminal surface of the graft. This technology could be used in the treatment of atherosclerosis disease and the design of new drug delivery systems.

L10 ANSWER 5 OF 9 BIOSIS COPYRIGHT 1997 BIOSIS

AN 94:311121 BIOSIS
DN 97324121
TI Efficient repopulation of denuded rabbit arteries with autologous ***genetically*** modified ***endothelial*** cells.
AU Conte M S; Birinyi L K; Miyata T; Fallon J T; Gold H K; Whittemore A D; ***Mulligan R C***
CS Whitehead Inst. Biomedical Res., 9 Cambridge Center, Cambridge, MA 02142, USA
SO Circulation 89 (5). 1994. 2161-2169. ISSN: 0009-7322
LA English
AB Background In an effort to determine whether specific ***genetic*** modifications of cells of the vascular system might improve the efficacy of existing clinical procedures such as endarterectomy, atherectomy, and percutaneous angioplasty, we investigated the utility of gene transfer to rapidly and efficiently repopulate injured arteries with ***genetically*** modified cells in an animal model. Methods and Results The method involves the harvest of autologous venous-derived ***endothelial*** cells, the efficient ***genetic*** modification of the cells through the use of recombinant retroviruses, and the subsequent implantation of the ***genetically*** modified cells on the surface of balloon-denuded arterial segments. With a rabbit model, freshly isolated ***endothelial*** cells were transduced with a recombinant retrovirus encoding the bacterial enzyme beta-galactosidase. The autologous transduced cells were then implanted on the surface of balloon denuded ileofemoral arterial segments at different cell densities; after 1 to 14 days, the animals were killed, and the ***vessel*** segments were examined. Cells expressing the bacterial gene product, as determined by in situ staining for beta-galactosidase, were found to be present on the surface of 28 of the 32 arteries seeded with ***genetically*** modified cells. ***Vessels*** examined at 4 to 7 days after seeding displayed 40% to 90% coverage with transduced cells, even when seeded at subconfluent density, and an intact ***endothelial*** cell monolayer, as evidenced by scanning electron microscopy studies. ***Vessels*** examined at 14 days after seeding revealed more variable staining for beta-galactosidase yet, again, in most cases, an intact ***endothelial*** cell monolayer. Conclusions These studies indicate the feasibility of generating segments of arterial ***vessels*** containing ***genetically*** modified cells in a rapid and efficient fashion, Further studies are now necessary to determine whether the local expression of specific polypeptides within a region of ***vessel*** for a finite period of time will be clinically useful.

L10 ANSWER 6 OF 9 EMBASE COPYRIGHT 1997 ELSEVIER SCI. B.V.
AN 95012996 EMBASE

TI Activities of granulocyte-macrophage colony-stimulating factor revealed by gene transfer and gene knockout studies.
AU Dranoff G.; ***Mulligan R.C.***
CS Dana-Farber Cancer Institute, Boston, MA, United States
SO Stem Cells, (1994) 12/SUPPL. (173-182).
ISSN: 1066-5099 CODEN: STCEEJ
CY United States
DT Journal
FS 015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 Cancer
025 Hematology
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LA English
SL English
AB We used retroviral mediated gene transfer and gene knockout technologies to explore the in vivo functions of murine granulocyte-macrophage colony-stimulating factor (GM-CSF). In tumor vaccination experiments, GM-CSF was the most potent molecule of a large number of cytokines, adhesion molecules and other immunomodulators for the induction of specific and long-lasting anti-tumor immunity. Vaccination required activities of both CD4 and CD8 positive lymphocytes, and likely involved the augmentation by GM-CSF of host professional antigen-presenting cell function. Mice engineered by homologous recombination techniques in embryonic stem cells to lack GM-CSF demonstrated no significant perturbations in steady-state hematopoiesis. All mutant animals, however, developed the accumulation of surfactant proteins and lipids in the alveolar space, the defining feature of the idiopathic human disorder pulmonary alveolar proteinosis. Surfactant lipid and protein content were increased in the absence of alterations in surfactant protein mRNA, supporting the concept that surfactant clearance or catabolism was perturbed. Extensive lymphoid hyperplasia associated with lung airways and blood ***vessels*** was also found, yet no infectious agents could be isolated. These results demonstrate that GM-CSF is not an essential growth factor for basal hematopoiesis and reveal an unexpected, critical role for GM-CSF in pulmonary homeostasis. It is tempting to speculate that the ability of GM-CSF to modulate the uptake and processing of particulate material underlies the mechanisms of immunostimulation and surfactant accumulation.

L10 ANSWER 7 OF 9 EMBASE COPYRIGHT 1997 ELSEVIER SCI. B.V.
AN 94176480 EMBASE
TI Involvement of granulocyte-macrophage colony-stimulating factor in pulmonary homeostasis.
AU Dranoff G.; Crawford A.D.; Sadelain M.; Ream B.; Rashid A.; Bronson

R.T.; Dickersin G.R.; Bachurski C.J.; Mark E.L.; Whitsett J.A.; ***Mulligan R.C.***

CS Department of Biology, Whitehead Biomedical Research Inst., Massachusetts Inst. of Technology, Cambridge, MA 02142, United States

SO SCIENCE, (1994) 264/5159 (713-716).
ISSN: 0036-8075 CODEN: SCIEAS

CY United States

DT Journal

FS 029 Clinical Biochemistry

LA English

SL English

AB The in vivo function of murine granulocyte-macrophage colony-stimulating factor (GM-CSF) was investigated in mice, carrying a null allele of the GM- CSF gene, that were generated by gene targeting techniques in embryonic stem cells. Although steady-state hematopoiesis was unimpaired in homozygous mutant animals, all animals developed the progressive accumulation of surfactant lipids and proteins in the alveolar space, the defining characteristic of the idiopathic human disorder pulmonary alveolar proteinosis. Extensive lymphoid hyperplasia associated with lung airways and blood ***vessels*** was also found, yet no infectious agents could be detected. These results demonstrate that GM-CSF is not an essential growth factor for basal hematopoiesis and reveal an unexpected, critical role for GM-CSF in pulmonary homeostasis.

L10 ANSWER 8 OF 9 EMBASE COPYRIGHT 1997 ELSEVIER SCI. B.V.

AN 94151062 EMBASE

TI Efficient repopulation of denuded rabbit arteries with autologous ***genetically*** modified ***endothelial*** cells.

AU Conte M.S.; Birinyi L.K.; Miyata T.; Fallon J.T.; Gold H.K.; Whittemore A.D.; ***Mulligan R.C.***

CS Whitehead Inst. of Biomedical Res., 9 Cambridge Center, Cambridge, MA 02142, United States

SO CIRCULATION, (1994) 89/5 (2161-2169).
ISSN: 0009-7322 CODEN: CIRCAZ

CY United States

DT Journal

FS 005 General Pathology and Pathological Anatomy
018 Cardiovascular Diseases and Cardiovascular Surgery

LA English

SL English

AB Background: In an effort to determine whether specific ***genetic*** modifications of cells of the vascular system might improve the efficacy of existing clinical procedures such as endarterectomy, atherectomy, and percutaneous angioplasty, we

investigated the utility of gene transfer to rapidly and efficiently repopulate injured arteries with ***genetically*** modified cells in an animal model. Methods and Results: The method involves the harvest of autologous venous-derived ***endothelial*** cells, the efficient ***genetic*** modification of the cells through the use of recombinant retroviruses, and the subsequent implantation of the ***genetically*** modified cells on the surface of balloon-denuded arterial segments. With a rabbit model, freshly isolated ***endothelial*** cells were transduced with a recombinant retrovirus encoding the bacterial enzyme .beta.-galactosidase. The autologous transduced cells were then implanted on the surface of balloon-denuded ileofemoral arterial segments at different cell densities: after 1 to 14 days, the animals were killed, and the ***vessel*** segments were examined. Cells expressing the bacterial gene product, as determined by in situ staining for .beta.-galactosidase, were found to be present on the surface of 28 of the 32 arteries seeded with ***genetically*** modified cells. ***Vessels*** examined at 4 to 7 days after seeding displayed 40% to 90% coverage with transduced cells, even when seeded at subconfluent density, and an intact ***endothelial*** cell monolayer, as evidenced by scanning electron microscopy studies. ***Vessels*** examined at 14 days after seeding revealed more variable staining for .beta.-galactosidase yet, again, in most cases, an intact ***endothelial*** cell monolayer. Conclusions: These studies indicate the feasibility of generating segments of arterial ***vessels*** containing ***genetically*** modified cells in a rapid and efficient fashion. Further studies are now necessary to determine whether the local expression of specific polypeptides within a region of ***vessel*** for a finite period of time will be clinically useful.

L10 ANSWER 9 OF 9 EMBASE COPYRIGHT 1997 ELSEVIER SCI. B.V.
AN 92197358 EMBASE
TI Repopulation of injured arteries with ***genetically*** modified ***endothelial*** cells.
AU Berinyi L.K.; Conte M.S.; ***Mulligan R.C.***
SO J. VASC. SURG., (1992) 15/5 (932-934).
ISSN: 0741-5214 CODEN: JVSUES
CY United States
DT Journal
FS 009 Surgery
018 Cardiovascular Diseases and Cardiovascular Surgery
029 Clinical Biochemistry
LA English

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9 MEDLINE
AN 95211017 MEDLINE
TI Activities of granulocyte-macrophage colony-stimulating factor revealed by gene transfer and gene knockout studies.
AU Dranoff G; ***Mulligan R C***
CS Dana-Farber Cancer Institute, Boston, Massachusetts.
SO STEM CELLS, (1994) 12 Suppl 1 173-82; discussion 182-4. Ref: 65
Journal code: BN2. ISSN: 1066-5099.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 9507
AB We used retroviral mediated gene transfer and gene knockout technologies to explore the in vivo functions of murine granulocyte-macrophage colony-stimulating factor (GM-CSF) [1, 2]. In tumor vaccination experiments, GM-CSF was the most potent molecule of a large number of cytokines, adhesion molecules and other immunomodulators for the induction of specific and long-lasting anti-tumor immunity. Vaccination required activities of both CD4 and CD8 positive lymphocytes, and likely involved the augmentation by GM-CSF of host professional antigen-presenting cell function. Mice engineered by homologous recombination techniques in embryonic stem cells to lack GM-CSF demonstrated no significant perturbations in steady-state hematopoiesis. All mutant animals, however, developed the accumulation of surfactant proteins and lipids in the alveolar space, the defining feature of the idiopathic human disorder pulmonary alveolar proteinosis. Surfactant lipid and protein content were increased in the absence of alterations in surfactant protein mRNA, supporting the concept that surfactant clearance or catabolism was perturbed. Extensive lymphoid hyperplasia associated with lung airways and blood ***vessels*** was also found, yet no infectious agents could be isolated. These results demonstrate that GM-CSF is not an essential growth factor for basal hematopoiesis and reveal an unexpected, critical role for GM-CSF in pulmonary homeostasis. It is tempting to speculate that the ability of GM-CSF to modulate the uptake and processing of particulate material underlies the mechanisms of immunostimulation and surfactant accumulation.

L10 ANSWER 2 OF 9 MEDLINE
AN 94236778 MEDLINE
TI Efficient repopulation of denuded rabbit arteries with autologous ***genetically*** modified ***endothelial*** cells.
AU Conte M S; Birinyi L K; Miyata T; Fallon J T; Gold H K; Whittemore A

D; ***Mulligan R C***

CS Whitehead Institute for Biomedical Research, Cambridge Center, MA 02142.

NC HL-41484 (NHLBI)
T32-GM-07560 (NIGMS)
HL-43771 (NHLBI)
SO CIRCULATION, (1994 May) 89 (5) 2161-9.
Journal code: DAW. ISSN: 0009-7322.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 9408

AB BACKGROUND: In an effort to determine whether specific ***genetic*** modifications of cells of the vascular system might improve the efficacy of existing clinical procedures such as endarterectomy, atherectomy, and percutaneous angioplasty, we investigated the utility of gene transfer to rapidly and efficiently repopulate injured arteries with ***genetically*** modified cells in an animal model. METHODS AND RESULTS: The method involves the harvest of autologous venous-derived ***endothelial*** cells, the efficient ***genetic*** modification of the cells through the use of recombinant retroviruses, and the subsequent implantation of the ***genetically*** modified cells on the surface of balloon-denuded arterial segments. With a rabbit model, freshly isolated ***endothelial*** cells were transduced with a recombinant retrovirus encoding the bacterial enzyme beta-galactosidase. The autologous transduced cells were then implanted on the surface of balloon-denuded ileofemoral arterial segments at different cell densities; after 1 to 14 days, the animals were killed, and the ***vessel*** segments were examined. Cells expressing the bacterial gene product, as determined by in situ staining for beta-galactosidase, were found to be present on the surface of 28 of the 32 arteries seeded with ***genetically*** modified cells. ***Vessels*** examined at 4 to 7 days after seeding displayed 40% to 90% coverage with transduced cells, even when seeded at subconfluent density, and an intact ***endothelial*** cell monolayer, as evidenced by scanning electron microscopy studies. ***Vessels*** examined at 14 days after seeding revealed more variable staining for beta-galactosidase yet, again, in most cases, an intact ***endothelial*** cell monolayer. CONCLUSIONS: These studies indicate the feasibility of generating segments of arterial ***vessels*** containing ***genetically*** modified cells in a rapid and efficient fashion. Further studies are now necessary to determine whether the local expression of specific polypeptides within a region of ***vessel*** for a finite period of time will

be clinically useful.

L10 ANSWER 3 OF 9 MEDLINE
AN 90296512 MEDLINE
TI ***Genetically*** modified ***endothelial*** cells in the treatment of human diseases.
AU Wilson J M; Birinyi L K; Salomon R N; Libby P; Callow A D; ***Mulligan R C***
CS Howard Hughes Medical Institute, University of Michigan Medical School, Ann Arbor 48109..
SO TRANSACTIONS OF THE ASSOCIATION OF AMERICAN PHYSICIANS, (1989) 102 139-47.
Journal code: W5P. ISSN: 0066-9458.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9010

L10 ANSWER 4 OF 9 MEDLINE
AN 89283716 MEDLINE
TI Implantation of vascular grafts lined with ***genetically*** modified ***endothelial*** cells.
AU Wilson J M; Birinyi L K; Salomon R N; Libby P; Callow A D; ***Mulligan R C***
CS Whitehead Institute, Cambridge, MA..
SO SCIENCE, (1989 Jun 16) 244 (4910) 1344-6.
Journal code: UJ7. ISSN: 0036-8075.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8909
AB The possibility of using the vascular ***endothelial*** cell as a target for gene replacement therapy was explored. Recombinant retroviruses were used to transduce the lacZ gene into ***endothelial*** cells harvested from mongrel dogs. Prosthetic vascular grafts seeded with the ***genetically*** modified cells were implanted as carotid interposition grafts into the dogs from which the original cells were harvested. Analysis of the graft 5 weeks after implantation revealed ***genetically*** modified ***endothelial*** cells lining the luminal surface of the graft. This technology could be used in the treatment of atherosclerosis disease and the design of new drug delivery systems.

L10 ANSWER 5 OF 9 BIOSIS COPYRIGHT 1997 BIOSIS
AN 94:311121 BIOSIS

DN 97324121
TI Efficient repopulation of denuded rabbit arteries with autologous ***genetically*** modified ***endothelial*** cells.
AU Conte M S; Birinyi L K; Miyata T; Fallon J T; Gold H K; Whittemore A D; ***Mulligan R C***
CS Whitehead Inst. Biomedical Res., 9 Cambridge Center, Cambridge, MA 02142, USA
SO Circulation 89 (5). 1994. 2161-2169. ISSN: 0009-7322
LA English
AB Background In an effort to determine whether specific ***genetic*** modifications of cells of the vascular system might improve the efficacy of existing clinical procedures such as endarterectomy, atherectomy, and percutaneous angioplasty, we investigated the utility of gene transfer to rapidly and efficiently repopulate injured arteries with ***genetically*** modified cells in an animal model. Methods and Results The method involves the harvest of autologous venous-derived ***endothelial*** cells, the efficient ***genetic*** modification of the cells through the use of recombinant retroviruses, and the subsequent implantation of the ***genetically*** modified cells on the surface of balloon-denuded arterial segments. With a rabbit model, freshly isolated ***endothelial*** cells were transduced with a recombinant retrovirus encoding the bacterial enzyme beta-galactosidase. The autologous transduced cells were then implanted on the surface of balloon denuded ileofemoral arterial segments at different cell densities; after 1 to 14 days, the animals were killed, and the ***vessel*** segments were examined. Cells expressing the bacterial gene product, as determined by in situ staining for beta-galactosidase, were found to be present on the surface of 28 of the 32 arteries seeded with ***genetically*** modified cells. ***Vessels*** examined at 4 to 7 days after seeding displayed 40% to 90% coverage with transduced cells, even when seeded at subconfluent density, and an intact ***endothelial*** cell monolayer, as evidenced by scanning electron microscopy studies. ***Vessels*** examined at 14 days after seeding revealed more variable staining for beta-galactosidase yet, again, in most cases, an intact ***endothelial*** cell monolayer. Conclusions These studies indicate the feasibility of generating segments of arterial ***vessels*** containing ***genetically*** modified cells in a rapid and efficient fashion, Further studies are now necessary to determine whether the local expression of specific polypeptides within a region of ***vessel*** for a finite period of time will be clinically useful.

L10 ANSWER 6 OF 9 EMBASE COPYRIGHT 1997 ELSEVIER SCI. B.V.
AN 95012996 EMBASE
TI Activities of granulocyte-macrophage colony-stimulating factor

revealed by gene transfer and gene knockout studies.
AU Dranoff G.; ***Mulligan R.C.***
CS Dana-Farber Cancer Institute, Boston, MA, United States
SO Stem Cells, (1994) 12/SUPPL. (173-182).
ISSN: 1066-5099 CODEN: STCEEJ
CY United States
DT Journal
FS 015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 Cancer
025 Hematology
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LA English
SL English
AB We used retroviral mediated gene transfer and gene knockout technologies to explore the in vivo functions of murine granulocyte-macrophage colony-stimulating factor (GM-CSF). In tumor vaccination experiments, GM-CSF was the most potent molecule of a large number of cytokines, adhesion molecules and other immunomodulators for the induction of specific and long-lasting anti-tumor immunity. Vaccination required activities of both CD4 and CD8 positive lymphocytes, and likely involved the augmentation by GM-CSF of host professional antigen-presenting cell function. Mice engineered by homologous recombination techniques in embryonic stem cells to lack GM-CSF demonstrated no significant perturbations in steady-state hematopoiesis. All mutant animals, however, developed the accumulation of surfactant proteins and lipids in the alveolar space, the defining feature of the idiopathic human disorder pulmonary alveolar proteinosis. Surfactant lipid and protein content were increased in the absence of alterations in surfactant protein mRNA, supporting the concept that surfactant clearance or catabolism was perturbed. Extensive lymphoid hyperplasia associated with lung airways and blood ***vessels*** was also found, yet no infectious agents could be isolated. These results demonstrate that GM-CSF is not an essential growth factor for basal hematopoiesis and reveal an unexpected, critical role for GM-CSF in pulmonary homeostasis. It is tempting to speculate that the ability of GM-CSF to modulate the uptake and processing of particulate material underlies the mechanisms of immunostimulation and surfactant accumulation.

L10 ANSWER 7 OF 9 EMBASE COPYRIGHT 1997 ELSEVIER SCI. B.V.
AN 94176480 EMBASE
TI Involvement of granulocyte-macrophage colony-stimulating factor in pulmonary homeostasis.
AU Dranoff G.; Crawford A.D.; Sadelain M.; Ream B.; Rashid A.; Bronson R.T.; Dickersin G.R.; Bachurski C.J.; Mark E.L.; Whitsett J.A.;